UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,577	06/26/2003	Molly Accola	FORS-08167	4684

23535 7590 05/05/2006

MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/606,577	ACCOLA ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *01 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15-19,22 and 23* is/are pending in the application.

4a) Of the above claim(s) *15-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed March 1, 2006. Currently, claims 1, 15-19, 22-23 are pending. Claims 15-19 have been withdrawn as drawn to non-elected subject matter.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

3. Any objections and rejections not reiterated below are hereby withdrawn.

4. This action contains new grounds of rejection necessitated by amendment.

Maintained Rejections

Priority

1. This application claims priority to US application 10/371,913, filed February 21, 2003 and provisional application 60/426,114, filed November 14, 2002.

Drawings

2. The drawings are acceptable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuber (US 5,834,181, November 10, 1998) in view of Fors et al. (Pharmacogenomics, Vol. 1, No. 2, pages 219-229, 2000) and Brow et al. (US Pat. 6,001,567, December 1999) and Zielenski et al. (Genbank Accession Number M55118, January 2001).

Shuber teaches high throughput screening methods for sequences or genetic alterations in nucleic acids. Shuber teaches a kit for carrying out high-throughput screening of nucleic acid samples. The kit includes, in packaged combination, at least the following components: a support, a multiplicity of purine and pyrimidine containing polymers, appropriate labeling components, and enzymes and reagents required for polymer sequence determination (col. 11, lines 55-62). Shuber teaches hybridization with allele-specific oligonucleotides (ASOs) for specific mutations. The allele specific oligonucleotides (ASOs) were 17mers synthesized and HPLC-purified. Shuber teaches examples of ASOs representing known cystic fibrosis mutations (co. 18, lines 42-45).

Shuber specifically teaches ASO probes for 2184delA (col. 19, lines 15). Thus, Shuber teaches a kit comprising a non-amplified detection assay configured for detecting CFTR allele 2184delA or the wild-type version thereof.

Fors teaches large-scale SNP scoring from unamplified genomic DNA. Fors teaches the Invader assay offers a simple diagnostic platform to detect single nucleotide changes with high specificity and sensitivity from unamplified, genomic DNA. The Invader assay uses a structure-specific 5' nuclease (or flap endonuclease) to cleave sequence-specific structures in each of two cascading reactions. The cleavage structure forms when two synthetic oligonucleotide probes hybridize in tandem to a target. Fors teaches that the signal amplification permits identification of single base changes directly from genomic DNA without prior amplification (abstract). The Invader technology is in routine use today for high-throughput SNP screening. The technology involves a simple, cascading reaction that can detect mutations and SNPs directly from unamplified genomic DNA or RNA in a homogeneous, isothermal, FRET-based format (page 222). Figure 1 illustrates the schematic of the Invader assay which contains various oligonucleotides including an oligonucleotide which comprises various 5' and 3' poritions that do not hybridize to target sequences. The technology is readily adapted to different sequences since the unlabeled analyte-specific oligonucleotides used in the primary reaction; no new dye-labelled oligonucleotides are needed (page 223, col. 1). This creates a streamlined approach to creating new assays allows rapid and accurate synthesis, purification and quantification of new SNP assay sets.

Further, Brow teaches an Invader cleavage assay in which both the first and second oligonucleotides are completely complementary to the target RNA. In another embodiment, the first oligonucleotide is partially complementary to the target RNA. In yet another embodiment, the second oligonucleotide is partially complementary to the target RNA. In yet another embodiment, both the first and the second oligonucleotide are partially complementary to the target RNA. The second oligonucleotide is partially complementary to the target sequence; the 3' end of the second oligonucleotide is fully complementary to the target sequence while the 5' end is non-complementary and forms a single-stranded arm. The non-complementary end of the second oligonucleotide may be a generic sequence which can be used with a set of standard hairpin structures. The detection of different target sequences would require unique portions of two oligonucleotides: the entire first oligonucleotide and the 3' end of the second oligonucleotide. The 5' arm of the second oligonucleotide can be invariant or generic in sequence.

Zielenski et al. Teaches the nucleotide sequence from the human cystic fibrosis transmembrane conductance regulator (CFTR) exon 13 where 2184delA is located.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the ASO solid support method of Shuber with the Invader method of Fors and Brow for detecting the 2184delA mutation in the cystic fibrosis gene depicted in Zielenski. The ordinary artisan would have been motivated to have detected the well known 2184delA mutation in the cystic fibrosis gene using the Invader assay. Fors specifically teaches the Invader method is a

simple diagnostic platform to detect single nucleotide changes with high specificity and sensitivity from unamplified, genomic DNA. For the expected benefits taught by Fors, the ordinary artisan would have been motivated to have modified the method of Shuber to obtain the claimed invention as a whole. Fors specifically teaches that the Invader technology is readily adapted to different sequences since the unlabeled analyte-specific oligonucleotides used in the primary reaction; no new dye-labelled oligonucleotides are needed (page 223, col. 1). This creates a streamlined approach to creating new assays allows rapid and accurate synthesis, purification and quantification of new SNP assay sets. The ordinary artisan would have been motivated to have detected alternative SNPs or mutations including the 2184delA mutation taught by Shuber as involved in cystic fibrosis for the benefit of quickly detecting a known mutation.

With regard to the second oligonucleotide sequence comprising SEQ ID NO: 85, given the very specific teachings in the specification regarding how to design the oligonucleotide sequences required for Invader directed assays. Brow specifically describes designing the oligonucleotides for the detection assay. Given the very specific mechanisms for Invader assays, design of the probes to the region of the mutation is required. Brow teaches the arms of the "flaps" are generic or invariant sequences. Given the full exon 13 sequence provided by Zielenski, the ordinary artisan would have been able to routinely design oligonucleotides which permit detection in the Invader assay. Furthermore, with regard to SEQ ID NO: 86 and 87, the ordinary artisan would have been motivated to have designed the "first" oligonucleotides

given the guidance in Brow for positioning of the oligonucleotides. As taught in Brow, the "flap" region which in non-complementary and forms a single-stranded arm may be generic sequence. Thus, the ordinary artisan would have been motivated to have generated any generic non-complementary arm. Thus, absent unexpected results the generic arm of SEQ ID NO: 86 and 87 would have been obvious.

Conclusion

5. No claims allowable over the art.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is

(571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg

Jeanine Goldberg
Primary Examiner
May 3, 2006